

WHAT IS CLAIMED IS:

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1. A nucleotide sequence comprising the nucleotide sequence of a virus belonging to the group of autonomous parvoviruses, and at least one effector nucleotide sequence which encodes an effector polypeptide ~~capable of effecting~~ <sup>which effects</sup> the destruction or the normalization of cancer cells or cells infected by virus, bacteria, or intracellular infectious parasites.

10 2. The nucleotide sequence according to claim 1, wherein the virus belongs to the group of oncosselective autonomous parvoviruses.

15 3. The nucleotide sequence according to claim 2, wherein the virus is chosen from the group consisting of the parvovirus H1, the fibrotropic parvovirus variant of the "Minute virus of Mice" (MVMp) and the parvovirus LuIII.

20 4. The nucleotide sequence according to claim 1, wherein the virus nucleotide sequence lacks nucleotide sequences encoding the parvovirus capsid proteins VP1 and VP2.

25 5. The nucleotide sequence according to claim 4, further comprising inserted between the promoter P4 and non-structural protein NSI, a promoter which is activated in target cells.

30 6. The nucleotide sequence according to claim 4, wherein the virus nucleotide sequence further lacks the nucleotide sequence of the promoter P38 and the nucleotide sequences encoding the parvovirus nonstructural proteins NSI and NSII.

7. The nucleotide sequence according to claim 1 wherein the effector nucleotide sequence comprises at least two coding and/or non-coding nucleotide sequences operably linked in polycistronic subunits under the control of a single promoter unit.

8. The nucleotide sequence according to claim 7, wherein the effector nucleotide sequence is between two coding nucleotide sequences and the effector nucleotide sequence comprises one IRES nucleotide sequence.

9. The nucleotide sequence according to claim 1, wherein the effector nucleotide sequence encodes at least one fusion polypeptide containing at least one ligand chosen from the group consisting of the hypervariable end specific of an antibody, a cytokine or a growth factor, wherein the ligand <sup>binds</sup> ~~is capable of binding~~ specifically to at least one molecule expressed at the surface of cancerous or infected cells.

10. The nucleotide sequence according to claim 1, wherein the effector nucleotide sequence comprises at least one sequence chosen from the group consisting of the nucleotide sequences that encode:

- a cytotoxic polypeptide or at least one fragment of this polypeptide,
- a molecule which confers on the transfected cell sensitivity to a toxic agent,
- at least one polypeptide or a fragment of this polypeptide which <sup>increases</sup> ~~is capable of~~ ~~increasing~~ an immune response,

- at least one polypeptide or a fragment of this polypeptide capable of inhibiting tumor neoangiogenesis.

5 11. The nucleotide sequence according to claim 10, wherein the fragment is fragment A of diphtheria toxin.

10 12. The nucleotide sequence according to claim 10, wherein the molecule is Herpes simplex virus type 1 thymidine kinase (HSV-TK), and the toxic agent is a guanosine analog labeled with the aid of radioisotopes which emit Auger electrons such as 123 Iodine.

15 13. The nucleotide sequence according to claim 10, wherein the polypeptide capable of inhibiting tumor neoangiogenesis is selected from the group consisting of interferon- $\alpha$ , interferon- $\beta$  and platelet factor 4.

20 14. The nucleotide sequence according to claim 1, wherein the effector nucleotide sequence comprises at least one nucleotide sequence which can be transcribed into an RNA, <sup>which destroys or</sup> ~~capable of destroying or~~ <sup>normalizes</sup> ~~of normalizing~~ cancer cells or infected cells.

25 15. The nucleotide sequence according to claim 14, wherein the nucleotide sequence that can be transcribed into an RNA capable of destroying or of normalizing cancer cells or infected cells is an antisense RNA or a ribozyme.

30 16. The nucleotide sequence according to claim 1 which further comprises at least one regulatory nucleotide sequence activated by - transactivation factors specific for a medical

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condition and/or for the affected cellular tissue  
and <sup>which cisactivating</sup> ~~capable of cisactivating~~ the effector nucleotide  
sequence.

5 17. The nucleotide sequence according to  
claim 16, wherein the regulatory nucleotide sequence  
contains all or part of the regulatory nucleotide  
sequence LTR of HIV viruses comprising the TAR  
sequence.

10 18. The nucleotide sequence according to  
claim 17, wherein the LTR nucleotide sequence lacks  
the enhancer nucleotide sequence NF-Kappa B trans-  
activable by cell factors and/or the nucleotide  
sequence NRE transactivable by the viral factor NEF.

15 19. The nucleotide sequence according to  
claims 16 or 17, which further contains a second  
regulatory nucleotide sequence consisting of all or  
part of the nucleotide sequence RRE and of the  
nucleotide sequence CRS of HIV viruses and of the  
adjacent splicing sites.

20 20. The nucleotide sequence according to  
claim 16, wherein the regulatory nucleotide sequence  
consists of a promoter "enhancer" nucleotide  
sequence specific for the cytomegalovirus and that  
the effector sequence is transcribed into a ribozyme  
25 ~~which specifically cleaves the messenger RNA~~  
~~encoding the cytomegalovirus  $\alpha$  protein.~~

30 21. The nucleotide sequence according to  
claim 16, wherein the regulatory nucleotide sequence  
contains at least one promoter and/or at least one  
enhancer transactivable in certain specific tissues  
and chosen from the group consisting of:

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- the nucleotide sequence controlling the expression of the gene encoding  $\alpha$ -fetoprotein (AFP),
- the nucleotide sequence controlling the expression of human placental protein 11 (PP11),

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- the nucleotide sequence controlling the expression of antigen CO - 029,
- the nucleotide sequence controlling the expression of antigen H23,
- the nucleotide sequence controlling the prostatic expression of prostatic secretory protein PSP94,

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- the nucleotide sequence controlling the expression of the protein pHGR11 associated with melanoma, ovarian cancer, adenocarcinoma of the colon and of the prostate,

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- the nucleotide sequence controlling the expression of protein pHGR74, expressed in the testicles, the prostate, the seminal vesicle and the granulosa of the ovary,

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- the sequences controlling the expression of proteins specific for the mammalian epithelium, for the uterine epithelium,

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- the nucleotide sequence controlling the expression of tyrosinase, expressed in the melanocytes and malignant melanoma,
- the sequences controlling the expression of elastase, expressed only in the exocrine pancreas,
- the nucleotide sequence controlling the hypophysial expression of prolactin and/or a mixture thereof.

22. The recombinant vector comprising the sequence or a portion of the sequence according to claim 1.

5 23. A pharmaceutical composition comprising a nucleotide sequence according to claim 1 and a pharmaceutical acceptable vehicle.

24. A pharmaceutical composition comprising the vector according to claim 22 and a pharmaceutically acceptable vehicle.

10 25. The pharmaceutical composition according to claim 24, which further comprises one or more wild-type viral agents belonging to the group of autonomous parvoviruses.

15 26. A method of treating cancer ~~or~~ ~~infections by virus, bacteria or intracellular infectious parasites~~ which comprises the step of administering to a patient an effective amount of vector containing the nucleotide sequence according to claim 1.

20 27. A method for treating cancer ~~or~~ ~~infection by virus or bacteria or intracellular infectious parasites~~, which comprises the step of administering to a patient an effective amount of a pharmaceutical composition according to claim 24.

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